

CLAIMS

What is claimed is:

1. An apparatus for disrupting cells or viruses, the
5 apparatus comprising:
 - a) a container having a chamber for holding the cells or viruses, wherein the container includes at least one flexible wall defining the chamber;
 - b) a transducer for impacting an external surface of
10 the flexible wall; and
 - c) a pressure source for increasing the pressure in the chamber.
2. The apparatus of claim 1, wherein the pressure source is
15 sufficient to increase the pressure in the chamber to at least 5 psi above the ambient pressure external to the container.
3. The apparatus of claim 1, wherein the pressure source is
20 sufficient to increase the pressure in the chamber to at least 15 psi above the ambient pressure external to the container.
4. The apparatus of claim 1, wherein the flexible wall
25 comprises a sheet or film of polymeric material.
5. The apparatus of claim 4, wherein the wall has a thickness in the range 0.025 to 0.1 mm.
- 30 6. The apparatus of claim 1, wherein the flexible wall comprises an elastomer.

7. The apparatus of claim 1, wherein the transducer comprises an ultrasonic horn.
8. The apparatus of claim 1, further comprising beads in the chamber for rupturing the cells or viruses.
9. The apparatus of claim 8, wherein the beads have a binding affinity for the cells or viruses to be disrupted.
10. The apparatus of claim 8, wherein the beads have a binding affinity for the intracellular material released from the disrupted cells or viruses.
11. The apparatus of claim 1, further comprising a first set of beads in the chamber for binding the cells or viruses and a second set of beads in the chamber for rupturing the cells or viruses.
12. The apparatus of claim 1, wherein the chamber has at least two ports positioned to permit flow of a fluid sample through the chamber, and wherein the apparatus further comprises at least one filter in the chamber for capturing the cells or viruses as the sample flows through the chamber.
13. The apparatus of claim 12, further comprising beads in the chamber.
14. A method for disrupting cells or viruses, the method comprising the steps of:
 - a) placing in the chamber of a container:

- i) the cells or viruses to be disrupted; and
- ii) a liquid;

wherein the container includes at least one flexible wall defining the chamber;

- b) placing a transducer against an external surface of the flexible wall;
- c) increasing the static pressure in the chamber; and
- d) impacting the flexible wall with the transducer to generate pressure pulses in the chamber.

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15. The method of claim 14, further comprising the step of agitating beads in the chamber to rupture the cells or viruses.

15 16. The method of claim 14, wherein the static pressure in the chamber is increased to at least 5 psi above the ambient pressure external to the container.

17. The method of claim 14, wherein the static pressure in
20 the chamber is increased to at least 15 psi above the ambient pressure external to the container.

18. The apparatus of claim 14, wherein the transducer
comprises an ultrasonic horn.

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19. The method of claim 14, wherein the step of placing the cells or viruses in the chamber comprises capturing the cells or viruses on at least one filter positioned in the chamber by forcing a fluid sample containing the
30 cells or viruses to flow through the chamber.

20. A device for use with a transducer to disrupt cells or viruses, the device comprising:

- a) a body defining a chamber, wherein the chamber is defined by at least one wall having an external surface for contacting the transducer;
- b) a filter stack positioned in the chamber for capturing the cells or viruses from a fluid sample as the sample flows through the chamber, wherein the filter stack comprises at least two filters having different average pore sizes, and wherein the filters are spaced from each other; and
- c) beads disposed between the filters.

21. The device of claim 20, wherein the filter stack comprises:

- a) a first filter;
- b) a second filter spaced from the first filter, the second filter having a smaller average pore size than the first filter; and
- c) a third filter spaced from the second filter, the third filter having a smaller average pore size than the second filter;

and wherein the device further comprises a first set of beads positioned between the first and second filters and a second set of beads positioned between the second and third filters.

22. The device of claim 21, wherein the beads in the first set have a different average diameter than the beads in the second set.

23. The device of claim 20, wherein the body further defines at least two ports to the chamber, and wherein the ports are positioned to permit continuous flow of the fluid sample through the chamber.

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24. The device of claim 20, wherein the wall for contacting the transducer comprises a sheet or film of polymeric material.

10 25. The device of claim 20, wherein the wall for contacting the transducer comprises an elastomer.

26. The device of claim 20, wherein the wall for contacting the transducer has a natural frequency higher than the
15 vibrating frequency of the transducer.

27. The device of claim 20, wherein the beads have a binding affinity for the cells or viruses to be disrupted.

20 28. The device of claim 20, wherein the beads have a binding affinity for the material released from the disrupted cells or viruses.

29. The device of claim 20, wherein the beads comprise a
25 first set of beads for binding the cells or viruses and a second set of beads for rupturing the cells or viruses.

30. An apparatus for disrupting cells or viruses, the
30 apparatus comprising:

- a) a container having a chamber for holding the cells or viruses, wherein the container includes at least one wall defining the chamber;
- b) a filter stack positioned in the chamber for capturing the cells or viruses from a fluid sample as the sample flows through the chamber, wherein the filter stack comprises at least two filters having different average pore sizes; and
- c) a transducer for contacting an external surface of the wall to generate pressure waves or pressure pulses in the chamber.

31. The apparatus of claim 30, wherein the transducer comprises an ultrasonic horn.

32. The apparatus of claim 30, further comprising beads disposed between the filters.

33. The apparatus of claim 30, wherein the body further defines at least two ports to the chamber, and wherein the ports are positioned to permit continuous flow of the fluid sample through the chamber.

34. The apparatus of claim 30, further comprising a pressure source for increasing the pressure in the chamber.

35. The apparatus of claim 34, wherein the wall comprises a sheet or film of polymeric material.

36. The apparatus of claim 30, wherein the wall has a natural frequency higher than the vibrating frequency of the transducer.

37. A method for disrupting cells or viruses, the method comprising the steps of:

- a) forcing a fluid sample containing the cells or viruses to flow through a chamber having a filter stack positioned therein, thereby capturing the cells or viruses on the filter stack, wherein the filter stack comprises at least two filters having different average pore sizes;
- b) placing a liquid in the chamber; and
- c) generating pressure waves or pressure pulses in the chamber by contacting a wall of the chamber with a vibrating transducer.

38. The method of claim 37, wherein the transducer comprises an ultrasonic horn.

39. The method of claim 37, further comprising the step of agitating beads between the filters.

40. The method of claim 37, further comprising the step of increasing the static pressure in the chamber.

41. An apparatus for disrupting cells or viruses, the apparatus comprising:

- a) a container having a chamber for holding the cells or viruses, wherein the container includes at least one wall defining the chamber;
- b) a transducer for contacting an external surface of the wall; and
- c) a support structure for holding the container and the transducer against each other such that the

transducer contacts the external surface of the wall and for applying to the container or to the transducer a substantially constant force to press together the transducer and the wall.

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42. The apparatus of claim 41, wherein the support structure comprises:

- a) a base;
- b) a first holder attached to the base for holding the
10 transducer;
- c) a second holder slidably mounted to the base for holding the container and for positioning the container against the transducer such that the external surface of the wall contacts the
15 transducer; and
- d) at least one elastic body for applying to the second holder the substantially constant force to press the wall against the transducer.

20 43. The apparatus of claim 41, wherein the support structure comprises:

- a) a base structure, wherein the transducer is slidably mounted to the base structure;
- b) a holder attached to the base structure for holding
25 the container such that the external surface of the wall contacts the transducer; and
- c) at least one elastic body for applying to the transducer the substantially constant force to press the transducer against the wall.

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44. The apparatus of claim 41, wherein the chamber is defined by:

- a) a first wall for contacting the transducer, wherein the first wall is sufficiently flexible to conform to a surface of the transducer;
 - b) a second wall spaced apart from the first wall, wherein the second wall is sufficiently flexible to move inwardly or outwardly in response to dynamic pressure changes in the chamber; and
 - c) a rigid frame defining the side walls of the chamber, wherein the side walls connect the flexible walls to each other;
- and wherein the support structure includes a holder for holding the frame such that the flexible walls are substantially unrestrained by the holder.

45. The apparatus of claim 44, wherein the holder comprises a body having a recess for receiving the frame and having an opening adjacent the recess, the opening being positioned to permit the outward expansion of the second wall when the container is positioned in the recess.

46. The apparatus of claim 41, wherein the transducer comprises an ultrasonic horn having a tip for contacting the wall, and wherein the thickness of the chamber is less than or equal to half of the diameter of the tip.

47. The apparatus of claim 41, wherein the container includes a port and a channel connecting the port to the chamber, and wherein the apparatus further comprises a plunger that is inserted into the channel to increase pressure in the chamber.

48. The apparatus of claim 47, wherein the plunger has a pressure stroke sufficient to increase the pressure in the chamber to at least 2 psi above the ambient pressure external to the container.

5 49. The apparatus of claim 41, wherein the wall comprises a sheet or film of polymeric material.

50. The apparatus of claim 41, wherein the force is in the
10 range of 2 to 5 lbs.

51. The apparatus of claim 41, wherein the force is at least 1 lb.

15 52. The apparatus of claim 41, further comprising beads in the chamber.

53. The apparatus of claim 41, wherein the chamber has at least two ports positioned to permit flow of a fluid
20 sample through the chamber, and wherein the apparatus further comprises at least one filter in the chamber for capturing the cells or viruses as the sample flows through the chamber.

25 54. The apparatus of claim 53, further comprising beads in the chamber.

55. An apparatus for disrupting cells or viruses that are placed in a chamber of a container, wherein the
30 container includes at least one wall defining the chamber, the apparatus comprising:

- a) a transducer for contacting an external surface of the wall and for generating pressure waves or pressure pulses in the chamber; and
- b) a support structure for holding the container and the transducer against each other such that the transducer contacts the wall and for applying to the container or the transducer a substantially constant force to press together the transducer and the wall.

56. The apparatus of claim 55, wherein the support structure comprises:

- a) a base structure, wherein the transducer is slidably mounted to the base structure;
- b) a holder attached to the base structure for holding the container such that the external surface of the wall contacts the transducer; and
- c) at least one elastic body for applying to the transducer the substantially constant force to press the transducer against the wall.

57. The apparatus of claim 55, wherein the transducer comprises an ultrasonic horn having a tip for contacting the wall.

58. The apparatus of claim 55, wherein the force is in the range of 2 to 5 lbs.

59. The apparatus of claim 55, wherein the force is at least 1 lb.

60. A method for disrupting cells or viruses, the method comprising the steps of:

- a) placing in the chamber of a container:
 - i) the cells or viruses to be disrupted; and
 - ii) a liquid;
- b) holding a transducer against a wall of the chamber;
- 5 c) applying to the container or to the transducer a substantially constant force to press together the transducer and the wall; and
- d) activating the transducer to generate pressure waves or pressure pulses in the chamber.

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61. The method of claim 60, further comprising the step of agitating beads in the chamber.

15 62. The method of claim 60, wherein the transducer comprises an ultrasonic horn having a tip for contacting the wall of the chamber, and wherein the thickness of the chamber is less than or equal to half of the diameter of the tip.

20 63. The method of claim 60, wherein the force is in the range of 2 to 5 lbs.

64. The method of claim 60, wherein the force is at least 1 lb.

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65. The method of claim 60, wherein the step of activating the transducer comprises inducing the transducer to vibrate, thereby imparting motion to the wall.

30 66. The method of claim 65, wherein the transducer vibrates at a frequency lower than the natural frequency of the wall.

67. The method of claim 60, wherein the container includes at least one solid support in the chamber, and the method further comprises the step of forcing a fluid sample containing the cells or viruses to flow through the chamber, thereby capturing the cells or viruses on the solid support.

68. An apparatus for disrupting cells or viruses, the apparatus comprising:

- a) a container having a chamber for holding the cells or viruses, wherein the container includes at least one wall defining the chamber; and
- b) a transducer for contacting an external surface of the wall and for vibrating at a frequency sufficient to generate pressure waves in the chamber, wherein the natural frequency of the wall is greater than the vibrating frequency of the transducer.

69. The apparatus of claim 68, wherein the ratio of the natural frequency of the wall to the vibrating frequency of the transducer is at least 2:1.

70. The apparatus of claim 68, wherein the ratio of the natural frequency of the wall to the vibrating frequency of the transducer is at least 4:1.

71. The apparatus of claim 68, wherein the wall is sufficiently deformable to deflect a distance in the range of 5 to 40 μm when the transducer applies a force in the range of 1 to 10 lbs. to the wall.

72. The apparatus of claim 68, wherein the wall is sufficiently deformable to deflect a distance in the range of 5 to 40 μm when the transducer applies a force in the range of 2 to 5 lbs. to the wall.
73. The apparatus of claim 68, wherein the wall is dome-shaped and convex with respect to the transducer.
74. The apparatus of claim 68, wherein the wall includes stiffening ribs.
75. The apparatus of claim 74, wherein the ribs extend radially from a central portion of the wall.
76. The apparatus of claim 68, wherein the transducer comprises an ultrasonic horn.
77. The apparatus of claim 68, further comprising beads in the chamber for rupturing the cells or viruses.
78. The apparatus of claim 68, further comprising a support structure for holding the container and the transducer against each other such that the transducer contacts the external surface of the wall and for applying to the container or to the transducer a substantially constant force to press together the transducer and the wall.
79. A method for disrupting cells or viruses, the method comprising the steps of:
- a) placing in the chamber of a container:

- i) the cells or viruses to be disrupted; and
- ii) a liquid;

wherein the container includes at least one wall defining the chamber;

- b) generating pressure waves in the chamber by contacting an external surface of the wall with a vibrating transducer, wherein the natural frequency of the wall is greater than the vibrating frequency of the transducer.

80. The method of claim 79, further comprising the step of agitating beads in the chamber.

81. The method of claim 79, further comprising the step of applying to the container or to the transducer a substantially constant force to press together the transducer and the wall.

82. The method of claim 81, wherein the force is in the range of 2 to 5 lbs.